Clinical trial results:
Efficacy of Cannabidiol in Treatment of Pain due to symptomatic Osteoarthritis of the Knee: A randomized, double-blind, placebo-controlled

Summary

EudraCT number	2019-003591-40
Trial protocol	AT
Global end of trial date	29 March 2022

Results information

Result version number	v1 (current)
This version publication date	23 October 2024
First version publication date	23 October 2024
Summary attachment (see zip file)	Cannabidiol Osteoarthristis Knee (CBD_KOA.pdf)

Trial information

Trial identification

Sponsor protocol code	131082019

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04607603
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Medical University of Vienna
Sponsor organisation address	Waehringer Guertel 18-20, Vienna, Austria,
Public contact	Universitätsklinik für Anästhesie, Medizinische Universität Wien, +43 14040041440, sibylle.pramhas@meduniwien.ac.at
Scientific contact	Universitätsklinik für Anästhesie, Medizinische Universität Wien, +43 14040041440, sibylle.pramhas@meduniwien.ac.at

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 December 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 March 2022
Global end of trial reached?	Yes
Global end of trial date	29 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Objective/Hypothesis
To evaluate the efficacy of cannabidiol in reducing pain due to knee osteoarthritis, as compared to placebo.
Efficacy will be evaluated using the Western Ontario and McMasters Universities Osteoarthritis Index (WOMAC) Pain score.

Protection of trial subjects:

Informed consent of subjects
Following comprehensive instruction regarding the nature, significance, impact and risks of this clinical trial, the patient must give written consent to participation in the study.
During the instruction the trial participants are to be made aware of the fact that they can withdraw their consent – without giving reasons – at any time without their further medical care being influenced in any way.
In addition to the comprehensive instructions given to the trial participants by the Investigator, the trial participants also receive a written patient information sheet in comprehensible language, explaining the nature and purpose of the study and its progress.
The patients must agree to the possibility of study-related data being passed on to relevant authorities.
The patients must be informed in detail of their obligations in relation to the trial participants insurance in order not to jeopardize insurance cover.
Acknowledgement / approval of the study
The Investigator (or a designated CRO) will submit this protocol and any related document provided to the subject (such as subject information used to obtain informed consent) to an Ethics Committee (EC) or Institutional Review Board (IRB). Approval from the committee must be obtained before starting the study.
The clinical trial shall be performed in full compliance with the legal regulations according to the Drug Law (AMG - Arzneimittelgesetz) of the Republic of Austria.

An application must also be submitted to the Austrian Competent Authorities (Bundesamt für Sicherheit im Gesundheitswesen (BASG) represented by the Agency for Health and Food Safety (AGES Medizinmarktaufsicht) and registered to the European Clinical Trial Database (EudraCT) using the required forms. The timelines for (silent) approval set by national law must be followed before starting the study.

Background therapy:

Parcetamol 3g per die

Evidence for comparator: -

Actual start date of recruitment	01 October 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 86
Worldwide total number of subjects	86
EEA total number of subjects	86

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	56
From 65 to 84 years	28
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Recruitment was conducted from October 1, 2020 to December 16, 2021.
Patients were recruited at the Outpatient Clinic of the Department of Special Anaesthesia and Pain Therapy at
the Medical University of Vienna, by advertisement in news print and via social media platforms.

Pre-assignment

Screening details:

Patients aged over 18–98 years with chronic knee pain were eligible. Patients were required to score ≥5 on the
pain subscale of the Western Ontario and McMasters Universities Osteoarthritis Index (WOMAC). Patients also had to fulfill the ACR clinical criteria for KOA

Period 1

Period 1 title	Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

Study medication for the entire study period was uniformly packaged and numbered by Hubertus Pharmacy (Spittal/Drau, Austria) that was not otherwise involved in the study. All study medication was delivered to Outpatient Clinic of the Department of Special Anaesthesia
and Pain Therapy at the Medical University of Vienna prior to the initiation of the study in a single batch. Participants were randomized to receive a medication number.

Arms

Are arms mutually exclusive?	Yes
Arm title	Cannabidiol

Arm description:

Hemp-derived CBD (purity >99,8%) was extracted by BioSynthesis Pharma Group (BSPG) Ltd., Sandwich,
UK, then imported and formulated into capsules by the BSPG subsidiary Trigal Pharma GmbH, Austria. Cap-sules containing CBD (200 mg/capsule).

Patients in CBD arm received 600mg per die (200mg-200mg-200mg)

Arm type	Experimental
Investigational medicinal product name	CBD
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

200mg CBD/capsule
600mg per die (1-1-1)

Arm title	Placebo

Arm description:

Ingredients: Fat, Ascorbyl Pamitate (E304), gelatine capsules (gelatine, titandioxide and/or other approved food colouring) Manufacturer: Hubertus Apotheke, Spital/Drau, Austria

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

3 per die (1-1-1)

Number of subjects in period 1	Cannabidiol	Placebo
Started	43	43
Completed	27	31
Not completed	16	12
Consent withdrawn by subject	1	1
Adverse event, non-fatal	9	5
Lost to follow-up	2	1
Lack of efficacy	4	1
Protocol deviation	-	4

Baseline characteristics

Reporting groups	
Reporting group title	Cannabidiol
Reporting group description:	
Hemp-derived CBD (purity >99,8%) was extracted by BioSynthesis Pharma Group (BSPG) Ltd., Sandwich, UK, then imported and formulated into capsules by the BSPG subsidiary Trigal Pharma GmbH, Austria. Cap-sules containing CBD (200 mg/capsule). Patients in CBD arm received 600mg per die (200mg-200mg-200mg)	
Reporting group title	Placebo
Reporting group description:	
Ingredients: Fat, Ascorbyl Pamitate (E304), gelatine capsules (gelatine, titandioxide and/or other approved food colouring) Manufacturer: Hubertus Apotheke, Spital/Drau, Austria	

Reporting group values	Cannabidiol	Placebo	Total
Number of subjects	43	43	86
Age categorical Units: Subjects			
Adults (18-64 years)	34	23	57
From 65-84 years	8	19	27
85 years and over	1	1	2
Age continuous Units: years			
median	60.0	65	
inter-quartile range (Q1-Q3)	55.0 to 65.0	56 to 73	-
Gender categorical Units: Subjects			
Female	30	30	60
Male	13	13	26

Subject analysis sets	
Subject analysis set title	CBD
Subject analysis set type	Full analysis
Subject analysis set description: CBD-Treatment	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Placebo	

Reporting group values	CBD	Placebo	
Number of subjects	43	43	
Age categorical Units: Subjects			
Adults (18-64 years)	34	23	
From 65-84 years	8	19	
85 years and over	1	1	

Age continuous Units: years			
median	60.0	65.0	
inter-quartile range (Q1-Q3)	55.0 to 65.0	56.0 to 73	
Gender categorical Units: Subjects			
Female	30	30	
Male	13	13	

End points

End points reporting groups

Reporting group title	Cannabidiol
Reporting group description:	
Hemp-derived CBD (purity >99,8%) was extracted by BioSynthesis Pharma Group (BSPG) Ltd., Sandwich, UK, then imported and formulated into capsules by the BSPG subsidiary Trigal Pharma GmbH, Austria. Cap-sules containing CBD (200 mg/capsule). Patients in CBD arm received 600mg per die (200mg-200mg-200mg)	
Reporting group title	Placebo
Reporting group description:	
Ingredients: Fat, Ascorbyl Pamitate (E304), gelatine capsules (gelatine, titandioxide and/or other approved food colouring) Manufacturer: Hubertus Apotheke, Spital/Drau, Austria	
Subject analysis set title	CBD
Subject analysis set type	Full analysis
Subject analysis set description:	
CBD-Treatment	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Placebo	

Primary: Change in WOMAC pain subscale score from baseline

End point title	Change in WOMAC pain subscale score from baseline
End point description:	
End point type	Primary
End point timeframe:	
8 weeks	

End point values	Cannabidiol	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	43		
Units: Scale 1-10				
median (inter-quartile range (Q1-Q3))	2.5 (1.8 to 3.3)	2.4 (1.7 to 3.2)		

Statistical analyses

Statistical analysis title	analysis of covariance model
Statistical analysis description:	
The primary endpoint was analyzed using an analysis of covariance model with change from baseline to week 8 as dependent variable and randomization group,baseline score of WOMAC Pain and stratification variables as independent variables; least-squares means from this model and their group differences are re- ported with 95% confidence intervals (CI). Residual distributions were successfully checked for approximate	

normal distribution and potentially influential observations
tions.

Comparison groups	Cannabidiol v Placebo
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	ANCOVA

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: From the start to the end	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1

Frequency threshold for reporting non-serious adverse events: 0 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: The template requires that number of subjects per reporting group that experienced a non-serious adverse events be given. However we reported total frequency of non-serious adverse per reporting group in our study.
CBD: 39 subjects at least one AE; Placebo 36 subjects at least one AE

Frequencies:	CBD	Placebo
Diarrhea	19	20
Elevation of ASAT, ALAT, gamma-GT	15	5
Abdominal pain	14	11
Fatigue	14	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported